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Case Report

A rare case of steroid 11 beta-hydroxylase deficiency in a child revealed by acute pulmonary edema

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Abstract

We report the case of a 5-year-old boy diagnosed with congenital adrenal hyperplasia due to 11-hydroxylase deficiency, revealed by disorders of sex development (DSD) and acute pulmonary edema due to severe hypertension. We considered the diagnosis based on biological and radiological examinations. The sociocultural background and the delayed diagnosis had a significant impact on the therapeutic decisions. All babies should be screened for 11 beta-hydroxylase deficiency, there should be specialized and interdisciplinary medical centers, and early detection is essential to avoiding serious complications of this disease.

INTRODUCTION

Congenital adrenal hyperplasia (CAH) due to 11β-hydroxylase deficiency is a rare autosomal recessive disease that represents only 5–8% of all CAH [1]. This frequency is significantly greater among several ethnic groups in North Africa and the Middle East due to consanguinity. It occurs from a CYP11B1 gene mutation that leads to hyperandrogenism and the accumulation of glucocorticoid and mineralocorticoid precursors [2]. The main clinical signs of the disease are sexual development disorders (DSD), precocious puberty, increased somatic growth, and hypertension, present in two out of every three patients with 11-hydroxylase deficiency [1, 3]. We report a case of a 5-year-old child, presented with 11β-hydroxylase deficiency, revealed by DSD and acute pulmonary edema due to severe hypertension, in whom the sociocultural environment had a substantial impact on the therapeutic decision.

CASE REPORT

A 5-year-old Moroccan child who had been raised as a boy, was brought into the pediatric emergency department with respiratory distress. He was the only child of a healthy consanguineous couple. He was born at home, and at the age of two, he had a posterior hypospadias repair surgery. At that time, no karyotype or other investigations were done. The parents report early development of pubic hair in this child. Also reported concerning family history of newborn death for unknown reason ten years ago. The patient had a fever, tachypnea, chest pain with cough, bilateral lung crackles, 90% oxygen saturation, and arterial hypertension of 180/100 mmHg (>99th percentile for age and height). The thoracic radiography revealed an image of acute pulmonary edema; therefore, we started adequate treatment immediately.

The patient weighed 27 kg (>97th centile for age, Standard deviation SD score: +3) and stood 128 cm (SD score: +4), he had a pubarche, noticed since childhood and was classified as Tanner stage 4, an abnormal external genitalia appearance with a 5.5-centimeter phallus-like organ in stretched length, a complete fusion of the labioscrotal folds, a single perineal orifice, hyperpigmented scrotum-like structure, non-palpable gonads, Prader Score IV (Fig. 1) and no mammary development. Furthermore, the patient's karyotype was 46 XX.

Biological tests revealed hypokalemia at 3 mmol/l, normal natremia, and glycemia, low cortisol at 200 ng/dl at 8 a.m., low plasma rennin activity at 40 ng/dl/h, low aldosterone at 3.31 ng/dl. On the other hand, levels of testosterone, androstenedione, and dehydroepiandrosterone were high, respectively, at 100 ng/dl, 850 ng/dl, and 1018 ng/dl. 17OH progesterone was moderately high at 845 ng/dl, with a very elevated deoxycorticosterone DOC dosage at 5619 ng/dl, 11-desoxycortisone at 13 340 ng/dl, and adrenocorticotropic hormone ACTH at 54,3 ng/dl.

There was a considerable bone age increase to 13 years for a chronological age of 5 using the Greulich and Pyle method. An abdominopelvic ultrasound (US) and magnetic resonance imaging (MRI) disclosed a uterine vestige with ovaries and follicles, without testicles (Figs 2 and 3).

Initial treatment of pulmonary edema and arterial hypertension of 180/100 mmHg (>99th percentile for age and height) for a baseline BP of 55–71 mmHg for diastolic BP, and 93–110 mmHg for systolic BP, which required hospitalization with constant

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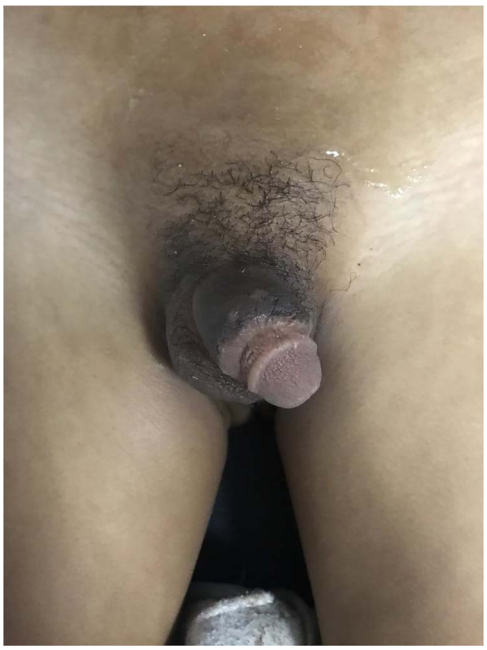

Figure 1. Clinical symptoms of ambiguous genitalia Prader Score IV.

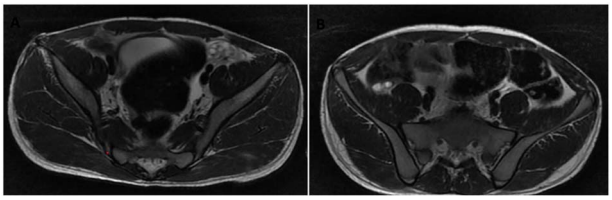

Figure 2. Magnetic resonance imaging (MRI) (transversal section) showing the left (**A**) and the right (**B**) ovary.

monitoring, intravenous Furosemide and intravenous Nicardipine (5 mg/h). After one week of treatment with amlodipine 5 mg daily and spironolactone 25 mg twice a day (1.85 mg/kg/day), we saw a regression to 110/91 mmHg. We initiated corticosteroid deficiency treatment with 10 mg/m2/day of hydrocortisone, and oral potassium supplements. The diagnosis' announcement was difficult because of the family's socioeconomic, and cultural context.

We provided the family with information about various treatments, they agreed to corticosteroid replacement therapy but refused surgery.

We allowed the patient to leave the hospital once his blood pressure had stabilized. Following a three-month follow-up, blood pressure was in the upper range, with a decrease in 11-deoxycortisol levels. Regrettably, the patient was lost during the follow-up.

DISCUSSION

DSD is a group of congenital conditions characterized by an abnormal gonad, chromosome, or anatomical sex organ development. Due to the ambiguity of the external genitalia, DSD can be observed at birth; however, diagnosis may be delayed until childhood or adulthood. The main symptoms are external genital virilization, precocious puberty, increased somatic growth, hirsutism, primary amenorrhea, and infertility [4, 5]. CAH is the most common cause of DSD, caused by a deficiency of enzymes or cofactors required for cortisol biosynthesis. 11β-hydroxylase deficiency represents 5–8% of all cases of CAH [1].

Children with this deficiency have low levels of cortisol and aldosterone, but high levels of androgens and mineralocorticoid precursors. As a result, they may have ambiguous genitalia, precocious puberty, accelerated growth, and hypertension, found in one-third to two-thirds of patients and is caused by DOC accumulation [1–3]. Later in childhood, hypertension is diagnosed and treated with spironolactone or amiloride alone or in combination with a calcium channel blocker [6].

In a recent study by Bang et al. on twenty-eight patients with 11β-OHD, prevalences of hypertension and hypertension-mediated organ damage (HMOD) were 100% and 50%, respectively. The most damaged organ were the kidneys, followed by the heart, eyes, and brain. Risk factors for HMOD were hypokalemia, blood pressure ≥180/110, and irregular glucocorticoid use [7].

The 11β-hydroxylase deficiency results in higher levels of DOC, 11-deoxycortisol, testosterone, and its precursors (dehydroepiandrosterone, DHEA, androstenedione), and lower levels of cortisol, renin, aldosterone, and corticosterone. In addition, our case had hypokalemia, which is uncommon in children. Genetic testing found mutations in the 11β-OH gene (CYP11B1) [8, 9].

Girls with non-classic 11-OHD are so virilized that 70% of them had Prader 4 or 5 at the time of diagnosis [2]. In addition to the abnormal appearance of the external genitalia, the family noticed pubarche and accelerated growth at a young age. Unfortunately, due to the inaccessibility of a nearby medical center, and the fact that this condition is culturally taboo in such a conservative society [9], the family concluded that medical consultation was unnecessary for their child.

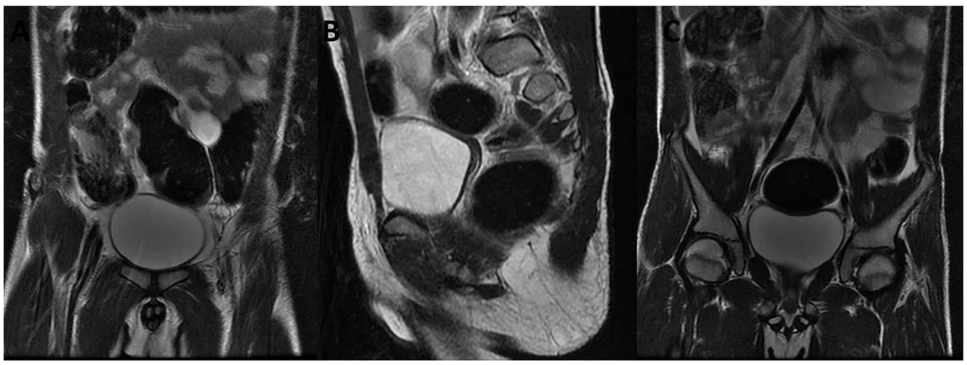

Figure 3. Magnetic resonance imaging (MRI) (sagittal section) shows the right (**C**), the left ovary (**A**) and uterus (**B**).

Medical orientation, in our opinion, may have also played a role in the outcome of this case. A karyotype and surgical exploration are required after performing a posterior hypospadias repair operation on a child with bilateral cryptorchidism [10].

Pediatricians, pediatric surgeons, and physicians need to be aware of the various stages of ambiguous genitalia for an early diagnosis and a better management.

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CONFLICT OF INTEREST STATEMENT

No conflicts of interest.

FUNDING

None.

ETHICAL APPROVAL

Not required for this case report.

CONSENT

A written and signed consent was provided by the patient's family to publish the findings of this case report.

GUARANTOR

Doctor Zohair El haddar.

REFERENCES

1. Bulsari K, Falhammar H. Clinical perspectives in congenital adrenal hyperplasia due to 11β-hydroxylase deficiency. *Endocrine* 2017;**55**:19–36.
2. Khattab A, Haider S, Kumar A, Dhawan S, Alam D, Romero R. *et al.* Clinical, genetic, and structural basis of congenital adrenal hyperplasia due to 11β-hydroxylase deficiency. *Proc Natl Acad Sci USA* 2017;**114**:E1933–40.
3. Zennaro MC, Boulkroun S, Fernandes-Rosa F. Inherited forms of mineralocorticoid hypertension. *Best Pract Res Clin Endocrinol Metab* 2015;**29**:633–45.
4. Lee PA, Nordenström A, Houk CP, Ahmed SF, Auchus R, Baratz A. *et al.* Global disorders of sex development update since 2006: perceptions, approach and care. *Horm Res Paediatr* 2016;**85**:158–80.
5. Beck MSE, Germano CW, Barros BA, Andrade JGR, Guaragna-Filho G, Paula GB. *et al.* Why pediatricians need to know the disorders of sex development: experience of 709 cases in a specialized service. *J Pediatr* 2020;**96**:607–13.
6. Breil T, Yakovenko V, Inta I, Choukair D, Klose D, Mittnacht J. *et al.* Typical characteristics of children with congenital adrenal hyperplasia due to 11β-hydroxylase deficiency: a single-Centre experience and review of the literature. *J Pediatr Endocrinol Metab* 2019;**32**:259–67.
7. Sun B, Lu L, Gao Y, Yu B, Chen S, Tong A. *et al.* High prevalence of hypertension and target organ damage in patients with 11β-hydroxylase deficiency. *Clin Endocrinol* 2022;**96**:657–65.
8. Valsalan R, Zimmermann A. Ambiguous genitalia and hypertension in a patient with congenital adrenal hyperplasia. *Intern Med J* 2013;**43**:334–7.
9. Yildiz M, Isik E, Abali ZY, Keskin M, Ozbek MN, Bas F. *et al.* Clinical and hormonal profiles correlate with molecular characteristics in patients with 11β-hydroxylase deficiency. *J Clin Endocrinol Metab* 2021;**106**:e3714–24.
10. van der Horst HJ, de Wall LL. Hypospadias, all there is to know. *Eur J Pediatr* 2017;**176**:435–41.